Invited Commentary

Invited Commentary: Identifying Women with Hypertension during Pregnancy—Is High Specificity Sufficient?

William M. Callaghan

From the Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA.

Received for publication August 6, 2006; accepted for publication August 9, 2006.

Hypertensive complications of pregnancy contribute to the burden of maternal morbidity and subsequently have an impact on neonatal morbidity and mortality. Although codes from the International Classification of Diseases should delineate the specific subtypes of pregnancy-related hypertension, how diagnoses are applied and how these codes are used in clinical settings are largely unknown. This commentary discusses the implications of using administrative codes to identify women with preeclampsia syndromes, especially when used to define outcomes or exposures for etiologic research.

hypertension; pregnancy; sensitivity and specificity; women


Hypertensive disorders are a leading cause of maternal mortality worldwide (1, 2). Moreover, although difficult to quantify, hypertensive complications of pregnancy contribute to the burden of maternal morbidity and subsequently have an impact on neonatal morbidity and mortality; in the United States, hypertension with first onset during pregnancy complicates 6–8 percent of pregnancies (3). The nomenclature of hypertension during pregnancy—gestational hypertension, transient hypertension of pregnancy, preeclampsia, severe preeclampsia—suggests the syndromic nature of this group of disorders. Women who are assigned one of the pregnancy-related diagnoses are defined by their clinical presentation rather than by markers of pathophysiologic change. As aptly stated by Dekker and Sibai (4), even an accurate diagnosis reflects meeting the “definition” of the assigned disorder without necessarily having a link to a pathologic consequence for the mother or neonate.

Gestational hypertension is defined as new onset of elevated blood pressure (≥140/≥90 mmHg) after the 20th week of pregnancy in a woman with no history of hypertension prior to pregnancy. Gestational hypertension is severe if there is sustained elevation of blood pressure (≥160/≥110). Most women with hypertension in pregnancy have gestational hypertension; this clinical presentation represents a group of women who have previously undiagnosed chronic hypertension, evolving preeclampsia, or transient hypertension of pregnancy. Transient hypertension of pregnancy is diagnosed postpartum in a woman with gestational hypertension without proteinuria who is normotensive by 12 weeks after delivery. Preeclampsia is defined as gestational hypertension with proteinuria. Severe preeclampsia occurs when there is severe gestational hypertension with proteinuria, when there is gestational hypertension with severe proteinuria, or when there is preeclampsia in the presence of multiorgan deterioration (3, 5–7). In theory, a specific code from the International Classification of Diseases (ICD) should delineate each of these entities. How diagnoses are applied and how these codes are used in clinical settings, however, are largely unknown. A survey of 33 of 34 obstetric departments in Denmark showed wide variability in diagnostic criteria and ICD reporting practices for preeclampsia (8). Geller et al. (9) reported an overall
positive predictive value of 54 percent when ICD, Ninth
Revision, codes were used to identify women with pre-
eclampsia. Although the positive predictive value for
eclampsia (preeclampsia with seizures) was low (42 per-
cent) in their study, if ICD, Ninth Revision, identified cases
eclampsia were included with ICD, Ninth Revision, iden-
tified cases of severe preeclampsia, the positive predictive
value was 87 percent.

Even when the code is accurately applied to the diagnosis,
what pathophysiologic entity is denoted and what is its con-
sequence? Adverse perinatal outcomes may be greater for
women with severe gestational hypertension than for
women with mild preeclampsia (10). Data from the National
Institute of Child Health and Human Development's Cal-
cium for Preeclampsia Prevention trial showed minimal im-
portance of mild gestational hypertension or mild preeclampsia
arising late in pregnancy; the mean birth weight in this
group exceeded the mean birth weight of infants born to
women with no hypertension (11). On the other hand, ma-
ternal and perinatal morbidity and mortality are consider-
able when women develop preeclampsia early in gestation;
it is not clear whether these entities represent the same
pathogenic mechanisms (12).

The etiologies of gestational hypertension and pre-
eclampsia are unknown; preeclampsia has been an area
of theories. Contemporary etiologic research has focused
on abnormal placentation with failure of the normal remod-
eling of maternal spiral arteries, maladaptive maternal-fetal
immunologic response, oxidative stress, dietary deficien-
cies, and genetic abnormalities (6, 7, 13, 14). Recent work
has focused on an imbalance in anti- and proangiogenic
factors (15–17). As might be expected for a syndrome with
such dynamic and nuanced nomenclature, multiple etiologic
hypotheses, and a lack of biomarkers for its pathophysi-
ology, no reliable predictors have been discovered, and pre-
vention trials have not been fruitful (4, 13, 18–20).

In addition to questions about the etiologies of the hyper-
tensive disorders of pregnancy, recent research has focused
on the association between preeclampsia and subsequent
health outcomes, particularly cardiovascular disease, in an
effort to explore the hypothesis that the predisposing path-
ophysiology for preeclampsia and heart disease might be
similar. Preeclampsia and atherosclerotic coronary disease
have common risk factors, including chronic hypertension,
obesity, insulin resistance, hypercholesterolemia, dyslipide-
dia, microalbuminuria, antiphospholipid syndrome, and
thrombophilies (21). Moreover, the association between
these entities is stronger for women with severe, early onset
preeclampsia or for women with preeclampsia that recurs in
successive pregnancies (22–24). This line of research re-
quires that preeclampsia be accurately identified as the ex-
posure. Thus, whether preeclampsia is the outcome or the
exposure of interest, there is a critical need to accurately
identify this entity, prospectively and retrospectively, in
large databases.

In this issue of the Journal, Klemmensen et al. (25) report
the validity of ICD, Tenth Revision, codes for the family of
pregnancy-related hypertensive disorders. Using the Danish
National Patient Registry as the source for codes and med-
ical record information from three hospitals as the “gold

standard” for diagnosis, they report low sensitivities for
all hypertensive disorders combined (49 percent) and for
individual subtypes (10–69 percent). The specificities of
codes from the ICD, Tenth Revision, were uniformly high
(>99 percent) for all hypertensive disorders combined and
for individual subtypes. Interview data specific to the data
collection methods of the Danish National Birth Cohort did
not substantially improve the findings, and information from
interviews could not discriminate between mild and severe
disease. On the basis of the high specificity of Danish Na-

tional Patient Registry data for hypertensive disorders,
Klemmensen et al. conclude that identifying cases by codes
from the ICD, Tenth Revision, is satisfactory for etiologic
studies where preeclampsia is the primary outcome or the
primary exposure. Given the scope of contemporary re-

search in this area, the challenges posed by the diagnosis
of hypertensive disorders in pregnancy, and the uncertainty
around their natural history, the data and conclusions from
this study merit discussion.

Misclassification of exposure and outcome plagues epi-
demiologic research. Do the findings of Klemmensen et al.
(25) provide reassurance for those who study the etiology of
preeclampsia or the sequelae of exposure to preeclampsia? In-
vestigations of the biology of hypertension in pregnancy
have advanced to a place where it is necessary to understand
the nuance of clinical presentation. It is increasingly impor-
tant to know when in gestation the woman presents with
her disease and the severity of disease at presentation and
pregnancy termination. Even though discharge data are spe-
cific for meeting a definition of the disease, they cannot provide
information that is sufficiently granular to accurately define
a case of preeclampsia for those involved in this realm of
research. Similarly, the burgeoning literature that reports
associations between subsequent cardiovascular disease and
severe, early onset, or recurrent hypertensive disorders calls
for research methods that capture both timing and severity of
pregnancy-associated hypertension.

Until or unless specific markers for the hypertensive dis-
orders of pregnancy become available, research will neces-
sarily depend upon the accurate characterization of disease
presentation. At best, accurately coding a defined presenta-
tion will include sufficient disease heterogeneity that, for
research purposes, can only be resolved by review of med-
ical records to confirm the diagnosis and to obtain the im-
portant details of the clinical presentation. The data from
this large study suggest something about the efficiency of
conducting such a study. For example, if one needed de-
tailed information to define and characterize cases of pre-
eclampsia as either the exposure or the outcome in a large
research setting, one could conceive of a large data set
(thousands) composed of administrative codes as a screening
test for the disease. In such a situation, review of all records
to confirm a diagnosis and glean the details of the clinical
presentation would impose an enormous burden. Given the
very high specificity reported by Klemmensen et al. (25), the
positive predictive value would be the pertinent test char-
acteristic to focus on, since the burden of record review re-
quires consideration of false positives. Klemmensen et al.
report that one in four records identified as having any de-
gree of preeclampsia did not have preeclampsia, and record

review would result in reclassification as a noncase or as nonexposed. Because the reported sensitivity is only moderate, a number of records will be misclassified as noncases or nonexposed. However, in the setting of a rare outcome, such misclassification will have minimal impact on measures of association. Although the allocation of resources for research involving this degree of record review may still be substantial, it likely represents a reasonable balance between diagnostic accuracy and workload in that only women who “screen positive” would require review of records.

This study was done in a small European country with a uniform health-care system; it may be premature to extrapolate these results to other settings. For now, the data reported by Klemmensen et al. (25) provide one example of how readily available data might be used and the caveats associated with their use. However, simply improving the specificity of identifying women who meet a definition of nonexposed. However, in the setting of a rare outcome, such misclassification will have minimal impact on measures of association. Although the allocation of resources for research involving this degree of record review may still be substantial, it likely represents a reasonable balance between diagnostic accuracy and workload in that only women who “screen positive” would require review of records.

This study was done in a small European country with a uniform health-care system; it may be premature to extrapolate these results to other settings. For now, the data reported by Klemmensen et al. (25) provide one example of how readily available data might be used and the caveats associated with their use. However, simply improving the specificity of identifying women who meet a definition of questionable relevance will do little to advance our understanding of this truly vexing and enigmatic group of disorders.

ACKNOWLEDGMENTS

The findings and conclusions in this report are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Conflict of interest: none declared.

REFERENCES